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**A PROSPECTIVE, MULTI-CENTRE OBSERVATIONAL COHORT STUDY OF TYPES OF  
ANALGESIA USED FOR PNEUMONECTOMY IN THE UK AND ITS ASSOCIATIONS  
WITH OUTCOME**

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## SUMMARY

### Background

Thoracic epidural analgesia was regarded as ‘the gold standard’ for prevention of pain associated with thoracotomy. Meta-analysis and systematic reviews of epidural versus paravertebral blockade for thoracotomy conclude that although the analgesia was comparable, paravertebral blockade had a better short-term side effect profile. However reduction in major complications including mortality has not been proven.

### Methods

The UK pneumonectomy study was a prospective observational cohort study. All UK thoracic surgical centres were invited to take part in the study. Data presented here relates to the mode of analgesia and outcome. The primary endpoint was suffering a major complication. Data were analysed for 312 patients having pneumonectomy over one calendar year of 2005, from 24 UK thoracic surgical centres.

### Results

The most common type of analgesia was epidural (61.1%) followed by paravertebral (31%). Epidural was associated with major complications (odds ratio 2.2, 95% confidence interval 1.1 - 3.8;  $P=0.02$ ) when analysed alongside patient and perioperative factors, in stepwise logistic regression analysis.

### Conclusions

This study has demonstrated an increased incidence of clinically important major post-pneumonectomy complications associated with thoracic epidural compared to paravertebral blockade technique. However, this study is unable to provide robust evidence to change clinical practice for a better clinical outcome. A large multicentre randomised controlled trial is now needed to compare the efficacy, complications and cost-effectiveness of epidural versus paravertebral blockade after major lung resection with the primary outcome for clinically important major morbidity

Key words: anaesthetic techniques ,epidural ; anaesthetic techniques ,paravertebral ; Surgery, thoracic; Postoperative Complications

Acute pain following thoracotomy can lead to cardio-respiratory complications as well as development of chronic pain. Thoracic epidural analgesia using local anaesthetic and opioid has been widely regarded as ‘the gold standard’ for prevention of pain associated with thoracotomy and for reduction of the associated complications. However, recent two meta-analysis and systematic reviews<sup>1</sup><sup>2</sup> comparing the analgesic efficacy and side effects of epidural versus paravertebral blockade for thoracotomy concluded that although the analgesia was comparable, paravertebral blockade had a better short-term side effect profile including a reduced incidence of urinary retention, hypotension, nausea and vomiting and pulmonary complications. This suggests that paravertebral blockade may be superior to epidural, but these reviews did not evaluate the most important outcomes (major complications including mortality). This prospective, national observational study of pneumonectomy outcome collected data on the types of analgesic techniques used and incidence of major complications. This will allow a more considered view of the optimal management of acute post-thoracotomy pain.

## **METHODS**

### **Study Design**

This was a prospective, multi-centre observational cohort study. All UK thoracic surgical centres (n=35 in 2005) were invited to take part in the study. Twenty-eight of these centres across the UK participated in this multi-centred ethics committee and local R&D approved study. A principal investigator at each site took responsibility of recruitment, data collection and follow up until hospital discharge. The more detailed study methodology was described in the paper ‘UK pneumonectomy outcome study (UKPOS): a prospective observational study of pneumonectomy outcome’.<sup>3</sup> The present study analyses further data from the UKPOS database.

### **Study Patients**

The inclusion criteria were all patients older than 18 years who underwent pneumonectomy for lung cancer in one calendar year (2005). Both planned pneumonectomy and on-table conversions from less radical pulmonary resection were included. The exclusion criteria were pneumonectomy for benign disease, pleuropneumonectomy, extended and completion pneumonectomy.

### **Data Collection**

Electronic data collection sheets were distributed to all investigators. Data collected included types of analgesic techniques as well as peri-operative patient, anaesthetic and surgical factors. In addition, data collected included fields to assess conformity between reporting centres. The data collection sheet is outlined in detail in Appendix 1. Once completed, the data sheet was transmitted to the data centre (Birmingham Heartlands Hospital) where it was checked for errors.

## **Outcome Measures**

The primary outcome was the development of a major complication, which was predefined a potential life-threatening complication requiring interventions or leading to death. Major complications included the following: significant arrhythmias requiring anti-arrhythmias, noteworthy haemodynamic instability requiring inotropes, severe respiratory complications requiring mechanical support (CPAP, non-invasive or invasive ventilation), unexpected ICU admissions, further surgery or 30 day mortality.

## **Statistical Analysis**

An independent senior statistician analysed the data using SPSS Statistics version 17.0 software (SPSS Inc, Chicago, USA). Data were tested for normality using Shapiro-Wilk's W test. The quantitative variables were analysed using the unpaired t test and Mann Whitney U test for normally and non-normally distributed data respectively. The categorical data were analysed by the Chi-squared test, Fisher's exact test and Mann Whitney U test as appropriate. Associations between analgesia techniques and major complications were tested with stepwise logistic regression analysis; taking into account commonly reported risk factors: age, ASA grades, pre-operative lung functions, airway pressures during one lung ventilation, types of analgesia and fluid management, for major complications following pneumonectomy. A P value of less than 0.05 was considered statistically significant. Data were presented as median (inter-quartile range), mean (SD) or as a number (%).

## **RESULTS**

The data centre received information for 312 patients from 24 centres distributed across the UK. Another four centres with site specific approval did not perform any pneumonectomies during the study period. Ninety two percent of the thoracic surgical centres were teaching hospitals.

### **Types of analgesia**

Data on types of analgesic techniques were available for 98.1% of cases (n=306). The most common type of analgesia was epidural (n=187, 61.1%) followed by paravertebral blockade (n=95, 31%). The other 7.8% of patients had alternative types of analgesia, which included patient controlled analgesia (4.9%), intrathecal morphine (1.6%) and intravenous morphine (1.3%). 78.9% of patients who received paravertebral blockade also received systemic opioids via patient controlled analgesia. 5.3% of cases had paravertebral blockade combined with intrathecal morphine. The systemic analgesic adjuncts used were as followed in percentage of all patients: paracetamol 60.3%, non-steroidal anti-inflammatory drugs 21.5%, tramadol 18%, nefopam 8%, codeine based preparations 18%, pethidine 0.3%. There were no differences between the epidural (n=146, 78% patients who received an

epidural) and paravertebral (n=72, 76% patients who received a paravertebral block) groups in use of non-steroidal anti-inflammatory drugs or paracetamol.

In the epidural group (n=187), a combination of epidural local anaesthetic and opioids was used in 62.6% of epidurals (n=117) whilst a combination of epidural local anaesthetic and systemic opioids was used in 3.2% of epidurals (n=6) and epidural opioids alone was used in 1.1% (n=2). However, for 33.2% (n=62) of epidurals the drug mixture used was not specified. For epidurals the most common local anaesthetic used was bupivacaine (concentration range 0.08 – 0.15%) and the most common opioid used was fentanyl (concentration range 2 – 10mcgml<sup>-1</sup>). In the paravertebral group (n=95), local anaesthetic alone was used in 46.3% of patients (n=43, 40% with 0.1 – 0.5% bupivacaine or 6.3% with lidocaine) whilst a mixture of bupivacaine with fentanyl was used in 6.3% of patients. However, for 47.4% (n=45) of patients the drug mixture used was not specified. The analgesic technique varied according to centre, 68.5% (n=128) of epidural analgesia was performed in the 12 centres where more than ten pneumonectomies (cases) per year were carried out. (p=0.002).

### **Patient characteristics**

As shown in Table 1, there were no differences in patient characteristics, ASA grade, co-morbidities or side of surgery between two groups. However, the patients that received paravertebral blockade weighed more than those that received epidural analgesia (p=0.04) although this difference did not reach statistical significance in terms of Body Mass Index (BMI) between two groups.

### **Pulmonary Function**

There were no significant differences in pre-operative or post-operative predicted pulmonary function between epidural and paravertebral groups as shown in Table 2.

### **Peri-operative management**

Table 3 shows most risk factors known to be associated with poor outcomes after lung surgery. The patients who had epidural analgesia had a significantly lower fluid balance per kilogram 24 hours post-operatively (p=0.003). There was a trend towards significant prolonged duration of surgery (p=0.07) and duration of one-lung ventilation (p=0.06) in the epidural analgesia group compared with paravertebral analgesia group. There was no significant difference between the two groups in location of post-operative care in a critical care area (ICU or HDU) or general ward. However, for critical care users, significant number of patients in the epidural group were transferred to Intensive Care Unit (level 3 care, 30/134, 18.3%) compared with 8.4% (7/76, P=0.003) in the paravertebral blockade group.

## **Mortality and Major Complications**

The in-hospital mortality was 4.8% (n=15) and the 30-day mortality 5.4% (n=17). Respiratory causes accounted for 58.8% of 30 day mortality (pneumonia, n=5; acute respiratory distress syndrome, n=3; pulmonary aspiration, n=1; and respiratory failure, n=1). Major haemorrhage accounted for 23.5% (n=4) and myocardial infarction for 17.6% (n=3). A total of 133 major complications occurred in 99 of 312 patients (31.7%).

In stepwise logistic regression analysis the use of epidural anaesthesia was found to be an independent risk factor for major complications (odds ratio (OR) 2.2, 95% confidence interval (CI) 1.1 to 3.8; p=0.02). The other factors that were associated with complications in stepwise logistic regression analysis were age (OR 1.07, CI 1.04 to 1.11; p=0.001), ASA (OR 1.7, CI 1.0 to 2.9; p=0.05) and DLCO (OR 0.78 (0.64 to 0.95; p=0.02). The incidence of major complications in the epidural and paravertebral groups is listed in Table 4.

## **DISCUSSION**

This study has shown that in the UK epidural blockade is the most popular method of analgesia for pneumonectomy (61.1%), followed by paravertebral blockade (31%). The rate of major complications associated with pneumonectomy was high at 31.7%, and this figure is similar to complication rates reported in the literature more than 10 years ago.<sup>4-7</sup>

The main strength of this study is that it is the largest prospective investigation into analgesia techniques and morbidity following elective pneumonectomy for cancer, and therefore the findings are representative of current UK practice. Moreover, the study was performed over one calendar year to reduce variability over time. The Society of Cardiothoracic Surgeons of Great Britain returns for 2005 – 2006 recorded 416 pneumonectomies for primary lung cancer, but this number would include completion or extended pneumonectomies not relevant to our study.<sup>8</sup> Our data capture of 312 pneumonectomies represent at least 75% of the case load performed in the UK in a calendar year. To our knowledge this is the largest prospective cohort study identifying that epidural blockade was associated with major complications in multiple logistic regression analysis.

### **Prevalence of analgesia techniques**

It is encouraging to see that either epidural or paravertebral blockade was used in most cases of pneumonectomy (92.1%) as these techniques have been shown to provide superior analgesia and less post-operative morbidity when compared with intravenous opioid techniques.<sup>7</sup> Thoracic epidural analgesia using local anaesthetic and opioid has been regarded world-wide as ‘the gold standard’ for managing acute post-thoracotomy pain, and our study has confirmed that this is the most common

analgesic technique in UK practice: over two-third patients were provided with thoracic epidural and 94% of these patients received a combination of local anaesthetic and opioid via epidural route. By contrast, 86% of paravertebral blocks used local anaesthetic alone but were combined with systemic opioid (PCA in 78.9% of cases) or spinal route (intrathecal morphine in 5.3% of cases).

### **Analgesia technique and pneumonectomy outcome**

The most interesting finding of this study was the increased incidence of major complications in the epidural group. The data have shown that the increased incidence of major complications for the epidural group is spread across complications, with increases in hypotension requiring inotropes, arrhythmias requiring antiarrhythmics, respiratory complications requiring ventilatory support and the need for further surgery in the epidural group contributing to the overall significant difference compared with paravertebral blockade. Some of these complications are known to be associated with epidural analgesia (such as hypotension) but others are not. The reason that paravertebral blockade may be associated with less hypotension and a reduction in pulmonary complications is because it is a unilateral technique and so respiratory and sympathetic function is preserved on the contra-lateral side.<sup>9</sup>

There were few significant differences between patient characteristics or peri-operative anaesthetic or surgical factors between groups. A surprising finding was that the epidural group received significantly less fluid at 24 hr than the paravertebral group (mean 14.8 vs 20.4 ml kg<sup>-1</sup>, P=0.003) though neither value is excessive. Although one might expect hypotension following bilateral sympathetic blockade to be managed by additional fluid it was possibly managed in this study by the increased use of inotropes in the epidural group (5.3% vs 1.1%). The duration of surgery, duration of one-lung ventilation and blood loss were not significantly different between the two groups indicating that difficulty of surgery cannot account for the higher complication rate in the epidural group. There was an association between type of analgesia and thoracic centre; the centres that performed more than ten pneumonectomies in the year were more likely to use epidural analgesia. There is therefore a possibility that the thoracic centre has confounded this result. One hypothesis is that the centres doing more cases are also operating on 'sicker patients'. However there were no differences between ASA grades, co-morbidities or lung function tests between epidural and paravertebral groups so this is unlikely to be the case. It is also unlikely to be related to the type of surgery as cases of pleuropneumonectomy, extended or completion pneumonectomy and pneumonectomy for benign disease were excluded from the study. Another explanation is that this association is due to differences in post operative care between centres. However this seems unlikely as 21/30 ICU admissions in the epidural group were from one thoracic centre. This probably is a consequence of



differences in training and analgesia protocols between study centres but these data were not collected.

### **Analgesia technique and locations of postoperative care**

It is expected that patients following pneumonectomy to be nursed in a critical care facility (ICU or HDU) for postoperative invasive monitoring regardless of type of analgesic technique provided.

However, there was approximate one in ten patients (11.3% -epidural vs 12.6% - PVB) directly sent to the general wards. Regarding critical care, we found a significant higher requirement for postoperative ICU care in epidural group compared with PVB group, which has cost implications in NHS. An Intensive Care Unit provides level 3 care (ref), at present, ICU costs £1,780 per bed per day and HDU costs £ 633 per bed per day (ref, please look at internet). In terms of post-operative management of different types of analgesic technique, use of PVB has potential benefits as post-operative management of epidural infusion requires critical care unit or a specialized ward whilst PVB can be managed on an ordinary ward.<sup>4 5</sup>

### **Comparison with other studies**

Davies et al recently published a meta-analysis comparing the analgesic efficacy and common side effects of epidural and paravertebral blockade.<sup>1</sup> They studied 520 adults from 10 randomised controlled trials undergoing thoracic surgery from 1989 to 2005. They found an increased incidence in common side effects associated with epidural analgesia when compared with paravertebral blockade. Paravertebral blockade was associated with less urinary retention, less hypotension, less nausea and vomiting and a reduction in pulmonary complications as well as higher successful rates. The small numbers in each study and the fact that most of the epidural infusions did not include opioids are both salient limitations to this meta-analysis.<sup>1</sup> In a more recent systematic review, after reviewing the randomised controlled trials evaluating regional techniques for post-thoracotomy analgesia (ref 8) between 1966 to 2004, Joshi et al confirmed that paravertebral blockade provided a significantly lower incidence of post-operative hypotension or pulmonary complications than thoracic epidural. These two reviews suggest that paravertebral blockade may be superior to epidural, but these reviews did not evaluate the most important outcomes (serious complications including mortality). To our knowledge, this cohort study is the largest worldwide prospective multi-centre investigation into analgesia techniques and major morbidity following elective pneumonectomy (UKPOS 2005), and the only study to quantify the comparisons of association of thoracic epidural or paravertebral block with clinically important major complications.

### **Limitations**

However, this study has some limitations. It is not a randomised controlled trial therefore has the inherent weakness of an observational study. As an observational study, the analgesia techniques were not standardised and certain variables were not measured adequately, for example, the efficacy of pain relief, the drug mixtures used or morphine consumption of each technique. Davies et al<sup>1</sup> in their systemic review concluded that technique failure rates were higher in the epidural group which may have partly accounted for the increase in side effects. The data of epidural failure rate was not available in our study, and it is possible the failure of epidurals led to inadequate analgesia which resulted in higher major complications in epidural group. Another potential confounding factor is the association of analgesia technique with thoracic surgical centre; epidural being more common in centres that perform more than 10 pneumonectomies per year. It is difficult to determine how much centre variation in practice may have influenced our result of epidural being associated with major complications. We are not able to say whether certain thoracic surgical centres have lower morbidity because they use paravertebral analgesia or whether it is due to unidentified confounding factors. Finally with the overall reduction in the number of pneumonectomies being performed as a percentage of lung resections over the last decade, the extrapolation of these results to patients with lesser resections becomes even more relevant.<sup>6</sup>

## **Conclusions**

This study has demonstrated an increased incidence of clinically important major post-pneumonectomy complications associated with thoracic epidural compared to paravertebral blockade technique. However, this study is unable to provide robust evidence to change clinical practice for a better clinical outcome. A large multicentre randomised controlled trial is now needed to compare the efficacy, complications and cost-effectiveness of epidural versus paravertebral blockade after major lung resection with the primary outcome for clinically important major morbidity.

**Table 1: Patient characteristics for epidural and paravertebral groups, (medians [ranges] or number of patients (%)) unless otherwise specified**

Characteristic	Epidural (n=187)	Paravertebral (n=95)	P value
Age (years)	62 [30-86]	65 [39-83]	0.08
Weight (kg)	70.5 [40-115]	76 [47-116]	0.04
Body mass index (kgm <sup>-2</sup> )	25 [16.6-41]	25.5 [18.8-37]	0.06
Male	119 (64.3%)	66 (73.3%)	0.17
ASA ≥3	76 (41.4%)	41 (45.6%)	0.52
Hypertension	65 (34.9%)	26 (28.9%)	0.34
Asthma/ COPD	42 (22.6%)	20 (22.2%)	1.00
Ischaemic heart disease	24 (12.9%)	18 (20%)	0.15
Diabetes	13 (7%)	8 (8.9%)	0.63
Myocardial infarction	12 (6.5%)	8 (8.9%)	0.47
Gastro-oesophageal reflux	12 (6.5%)	6 (6.7%)	1.00
Renal impairment	4 (4.4%)	4 (2.2%)	0.45
Heart failure	1 (0.5%)	0 (0%)	1.00
Neo-adjuvant therapy	17 (9.4%)	12 (13.3%)	0.40
Right sided procedures	66 (35.7%)	30 (33.3%)	0.79

COPD, chronic obstructive pulmonary disease; ASA, American Society of Anesthesiology

**Table 2: Pre-operative pulmonary function for epidural and paravertebral groups (medians and [ranges] unless otherwise specified)**

Pulmonary function	Numbers	Epidural	Paravertebral	P value
FEV <sub>1</sub> /FVC	174, 89	69 [41.3-90.5]	67.7 [37-100]	0.33
FEV <sub>1</sub>	186, 89	2.14 [0.82-4.1]	2.25 [0.49-3.66]	0.84
FEV <sub>1</sub> %	181, 87	78.9 [35.8-130.8]	77.7 [17.4-125.6]	0.47
ppo FEV <sub>1</sub> %	183, 89	40 [19-69.3]	39.1 [8.1-66.6]	0.55
DLCO	102, 40	5.6 [0.8-12.2]	6.3 [3.1-11.8]	0.30
DLCO %	106, 43	69 [29-136]	72 [39-112]	0.17
ppo DLCO %	105, 43	34.6 [15.3-71.6]	37 [20.5-53.1]	0.25
Pre-op saturations < 95%	21	16 (9.8%)	5 (7.8%)	0.80

FEV<sub>1</sub>, forced expiratory volume (l) in one second; FVC, forced vital capacity (l); FEV<sub>1</sub>% percentage of measured FEV<sub>1</sub> to predicted normal; ppo, predicted post-operative; DLCO, diffusion capacity for carbon monoxide needs unit .

**Table 3: Peri-operative management for epidural and paravertebral groups (median and [range] unless otherwise specified)**

Peri-operative management	Number	Epidural	Paravertebral	P value
Blood loss during surgery (ml)	187, 95	390 [200-700]	350 [200-700]	0.46
Fluid balance at 24hrs (ml kg <sup>-1</sup> )	174, 84	14.8 [-42.3-87.6]	20.4 [-6-62.5]	0.003
Duration of surgery (min)	182, 90	150 [67-460]	140.5 [75-330]	0.07
Duration of OLV (min)	172, 89	120 [40-450]	115 [45-270]	0.06
Plateau inspiratory pressure >25 cm H <sub>2</sub> O (vs ≤ 25)	155, 67	33 (21.2%)	15 (22.4%)	0.49
Pressure vs volume controlled ventilation)	178, 89	85 (47.5%)	37 (41.6%)	0.37
Converted procedure (vs planned)	186, 90	58 (31.2%)	32 (35.6%)	0.50
Stump closure with staples (vs sutures)	185, 67	163 (88.1%)	57 (85.1%)	0.53
Postop location ICU and HDU vs ward	185, 95	164 (88.7%)	83 (87.4%)	0.43
Post-op location – ICU vs HDU	164, 83	30 (18.3%)	7 (8.4%)	0.003

**Number indicates the number of patients in each group (epidural, paravertebral) with complete dataset in that field**

**Table 4: Incidence of major complications between epidural and paravertebral groups and length of hospital stay**

Complications	Epidural number patients (%) N=187	Paravertebral number patients (%) N=95	P value
Major complication	66 (35.3)	22 (23.1)	0.049
Arrhythmia	39 (20.9)	17 (18.9)	0.75
Atrial fibrillation	34 (18.2)	16 (17.8)	1.00
Hypotension needing inotropes	10 (5.3)	1 (1.1)	0.11
Respiratory	14 (7.5)	4 (4.4)	0.44
Unplanned ICU admissions	17 (9.1)	4 (4.4)	0.23
Further surgery	10 (5.3)	2 (2.2 )	0.35
30 day mortality	12 (6.4)	4 (4.2)	0.80
Length of hospital stay (days)	8 [1-63]	8 [4-27]	0.74

Length of hospital stay; median [range]

Declaration of interests: None

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## **APPENDIX 1**

### **Essential fields from data collection sheet**

Centre code  
Patient number  
Date of surgery  
Age of patient  
Gender  
Height (m)  
Weight (kg)  
BMI (kg/m<sup>2</sup>)  
Exercise capacity (distance on flat in metres)  
Alcohol intake (units per week)  
Ever smoked (yes/no)  
Pack year history (average number of cigarettes smoked per day divided by 20, multiplied by total number of years smoked)  
Time since stopped smoking (weeks)  
ASA physical status  
Co-morbidities (Include all cardiac, respiratory, renal and vascular history and any other potentially relevant past history)  
Pre-operative medication (Include steroids, NSAIDs, antifungals, leukotriene receptor antagonists, beta-2 agonists, and all 'cardiac drugs')  
Lung cancer stage (pre-operative)  
Cancer cell type  
Adjuvant chemo- or radiotherapy (what drugs/ radiation/ dose/ regime /and when)  
FEV<sup>1</sup> (actual value in litres), FEV<sup>1</sup> % (as percent of predicted value)  
FEV<sup>1</sup> / FVC (as percentage)  
DLCO (actual value), DLCO % (as percentage of predicted normal)  
KCO (actual value), KCO % (as percent of predicted normal)  
Arterial line inserted  
Central venous pressure line inserted  
Mini-trach or tracheostomy inserted (if so when inserted and time in-situ)  
Pressure or volume controlled ventilation (during surgery)  
Fluids given during surgery (list fluid given in millimetres and type of fluid given)  
Drugs given during surgery and during post-operative period (all non anaesthetic drugs, e.g. diuretics, inotropes, antibiotics not normally taken by patient, received during the first 48 hours post-operatively and for entire length of stay on ICU/HDU)  
Blood loss during surgery  
Planned or converted  
Duration of intermittent positive pressure ventilation (in minutes)  
Duration of one-lung ventilation (in minutes from initiation to completion of surgery)  
Duration of surgery (in minutes from skin incision to final suture)  
Initial post-operative location  
Unplanned ICU admission  
ICU length of stay (in days)  
Types of post-operative pain relief (state which drugs, regime and route)  
Fluids given after surgery in first 24 hours  
Output (fluid output during surgery up to 24 hours- include urine output, chest drain output and any other losses)  
Fluid balance (fluid balance at 24 hours post-operatively, give figure in millimetres and whether positive or negative)

Post-operative complications (list organ systems and exact complications for respiratory, cardiovascular, renal, hepatic systems, sepsis, multi-organ failure)  
 Post-pneumonectomy pulmonary oedema (diagnosed as hypoxia PF ratio < 40, bilateral infiltrates on chest x-ray, PAP < 18mmHg when measured, cardiac index > 3 when PiCCO or oesophageal Doppler used, PEEP requirement  $\geq$  7.5mmHg)  
 Survived to discharge  
 Length of stay in hospital (to death or discharge in days)  
 Cause of death (from death certificate or post mortem)

## APPENDIX 2

The UKPOS Centre Co-ordinators: *Clinical centres:* **Aberdeen Royal Infirmary, Aberdeen** – L. Strachan; **Barts and the London, London** – J. Nelson, V. Brown; **Birmingham Heartlands Hospital, Birmingham** – F. Gao; **Blackpool Victoria Hospital, Blackpool** – A. Knowles; **Cardiothoracic Centre, Liverpool** – J. Kendall; **Edinburgh Royal Infirmary, Edinburgh** – G. Bowler; **Freeman Hospital, Newcastle** – L. Pardeshi; **Glasgow Royal Infirmary, Glasgow** – M. Stockwell; **Glasgow Western Infirmary, Glasgow** – A. Macfie; **Guy's and St Thomas' Hospital, London** – A. Pearce; **Hairmyres Hospital, Hairmyres** – B. McCulloch; **Harefield Hospital, London** – J. Mitchell; **James Cook University Hospital, South Cleveland** – M. Foley; **Leeds General Infirmary, Leeds** – R. Mills; **Manchester Royal Infirmary, Manchester** – M. Forrest; **Morrison Hospital, Swansea** – M. Gilbert; **New Cross Hospital, Wolverhampton** – R. Giri; **Norfolk and Norwich University Hospital, Norwich** – N. Woodall; **Northern General Hospital, Sheffield** – D. Woodward; **Nottingham City Hospital, Nottingham** – J. Latter; **Royal Devon and Exeter Hospital, Exeter** – C. Berry; **University Hospital of Wales, Cardiff** – T. Dhallu; **Wessex Cardiothoracic Centre, Southampton** – L. Nel; **Wythenshaw Hospital, Manchester** – G. Lee.

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